IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IN RE: '318 PATENT INFRINGEMENT LITIGATION	)	C.A. No. 05-356 (KAJ)
	)	(consolidated)
	)	

NOTICE OF SUBPOENA FOR DEPOSITION AND PRODUCTION OF DOCUMENTS TO THE MOUNT SINAI HOSPITAL

To: Steven J. Balick
ASHBY & GEDDES
222 Delaware Avenue, 17th Floor
Wilmington, DE 19899

George F. Pappas
COVINGTON & BURLING
1201 Pennsylvania Avenue, N.W.
Washington, D.C. 20004

Steven P. Berman
Office of General Counsel
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933

PLEASE TAKE NOTICE that, pursuant to Rule 30 of the Federal Rules of Civil Procedure and as indicated in the attached subpoena (Ex. A), Defendants, by and through their attorneys, hereby give notice of their intention, to take the deposition upon oral examination on the date indicated of:

1. The Custodian of Records of The Mount Sinai Hospital on April 28, 2006.

This deposition will commence at **9:30 a.m. EST** on **April 28, 2006**, at the offices of Winston & Strawn LLP, 200 Park Avenue, New York, NY 10166-4193. The deposition will be taken before a notary public or other officer authorized to administer the oath

under law, and will continue day to day until completed with adjournments as to time and place that may be necessary. The deposition may be recorded by videographic and/or stenographic means.

NOTICE IS FURTHER GIVEN THAT The Mount Sinai Hospital is instructed to produce documents, identified in the Rider to the attached subpoena (Ex. A), at the offices of Winston & Strawn LLP, 35 West Wacker Drive, Chicago, IL 60601, on or before April 15, 2006.

If counsel for The Mount Sinai Hospital or Plaintiffs have any questions regarding this Notice, you are invited to contact any counsel for Defendants to discuss this matter.

/s/ Mary B. Matterer
Mary B. Matterer # 2696
MORRIS JAMES HITCHENS & WILLIAMS LLP
222 Delaware Ave., 10th Floor
Wilmington, DE 19801
Telephone: (302) 888-6800
Facsimile: (302) 571-1750
mmatterer@morrisjames.com

Of Counsel (admitted pro hac vice):
William A. Rakoczy
Christine J. Siwik
Amy D. Brody
RAKOCZY MOLINO MAZZOCHI SIWIK LLP
6 West Hubbard Street, Suite 500
Chicago, IL 60610
Telephone: (312) 527-2157
Facsimile: (312) 222-6321
wrakoczy@rmmslegal.com

Attorneys for Defendants/Counterclaim-Plaintiffs Mylan Pharmaceuticals Inc. and Mylan Laboratories Inc.

Dated: March 31, 2006

CERTIFICATE OF SERVICE

I hereby certify that on the 31st day of March, 2006, I caused a true and correct copy of the foregoing document, **NOTICE OF SUBPOENA FOR DEPOSITION AND PRODUCTION OF DOCUMENTS TO THE MOUNT SINAI HOSPITAL**, to be served upon the following counsel of record as indicated below:

Via Fed Ex® and E-mail: George F. Pappas *(gpappas@cov.com)* Christopher N. Sipes *(csipes@cov.com)* Jeffrey B. Elikan *(jelikan@cov.com)* Laura H. McNeill *(lmcneill@cov.com)* Joseph H. Huynh (*jhuynh@cov.com*) Uma N. Everett (*ueverett@cov.com*) Michael E. Paulhus (*mpaulhus@cov.com*) William D.A. Zerhouni (*wzerhouni@cov.com*) **COVINGTON & BURLING** 1201 Pennsylvania Avenue, N.W. Washington, D.C. 20004-2401 Telephone: (202) 662-6000 Facsimile: (202) 662-6291	**Via Hand Delivery and E-mail**: Steven J. Balick *(sbalick@ashby-geddes.com)* John G. Day *(jday@ashby-geddes.com)* **ASHBY & GEDDES** 222 Delaware Ave., 17th Fl. P.O. Box 1150 Wilmington, DE 19899 Telephone: (302) 654-1888 Facsimile: (302) 654-2067
Via Fed Ex® and E-mail: Steven P. Berman (*sberman@corus.jnj.com*) Office of General Counsel Johnson & Johnson One Johnson & Johnson Plaza New Brunswick, NJ 08933 Telephone: (732) 524-2805 Facsimile: (732) 524-5866	
Counsel for Plaintiffs Janssen Pharmaceutica N.V., Janssen, L.P. and Synaptech, Inc.	

Via E-mail:

Alan Bernstein *(abernstein@crbcp.com)* (x124) Mona Gupta *(mgupta@crbcp.com)* (x160) **CAESAR, RIVISE, BERNSTEIN, COHEN & POKOTILOW, LTD.** 1635 Market Street, 11th Floor Philadelphia, PA 19103-2212 Telephone: (215) 567-2010 Facsimile: (215) 751-1142	Frederick L. Cottrell, III *(cottrell@rlf.com)* Anne Shea Gaza *(gaza@rlf.com)* **RICHARDS, LAYTON & FINGER, P.A.** One Rodney Square P.O. Box 551 Wilmington, DE 19801 Telephone: (302) 651-7509 Facsimile: (302) 651-7701
Counsel for Defendant Alphapharm Pty Ltd.	

Daniel F. Attridge, P.C. *(dattridge@kirkland.com)* Edward C. Donovan *(edonovan@kirkland.com)* Karen M. Robinson *(krobinson@kirkland.com)* Corey J. Manley *(cmanley@kirkland.com)* **KIRKLAND & ELLIS LLP** 655 Fifteenth Street, N.W., Suite 1200 Washington, D.C. 20005-5793 Telephone: (202) 879-5000 Facsimile: (202) 879-5200	Josy W. Ingersoll *(jingersoll@ycst.com)* John W. Shaw *(jshaw@ycst.com)* Adam W. Poff *(apoff@ycst.com)* **YOUNG CONAWAY STARGATT & TAYLOR LLP** The Brandywine Building 1000 West St., 17th Floor P.O. Box 391 Wilmington, DE 19899-0391 Telephone: (302) 571-6600 Facsimile: (302) 571-1253
Counsel for Defendants Teva Pharmaceuticals USA and Teva Pharmaceuticals Industries Ltd.	

George C. Lombardi *(glombardi@winston.com)* Taras A. Gracey *(tgracey@winston.com)* Lynn M. Ulrich *(lulrich@winston.com)* Brian L. Franklin *(bfranklin@winston.com)* **WINSTON & STRAWN LLP** 35 West Wacker Dr. Chicago, IL 60601 Telephone: (312) 558-5000 Facsimile: (312) 558-5700	John C. Phillips. Jr. *(jcp@pgslaw.com)* Brian E. Farnan *(bef@pgslaw.com)* **PHILLIPS, GOLDMAN & SPENCE, P.A.** 1200 N. Broom St. Wilmington, DE 19806 Telephone: (302) 655-4200 Facsimile: (302) 655-4210
Counsel for Defendants Barr Laboratories, Inc. and Barr Pharmaceuticals, Inc.	

Robert J. Gunther, Jr. *(robert.gunther@lw.com)* James P. Barabas *(james.barabas@lw.com)* **LATHAM & WATKINS LLP** 885 Third Ave., Suite 1000 New York, NY 10022-4802 Telephone: (212) 906-1200 Facsimile: (212) 751-4864	Richard D. Kirk *(rkirk@bayardfirm.com)* **THE BAYARD FIRM** 222 Delaware Ave., Suite 900 P.O. Box 25130 Wilmington, DE 19899 Telephone: (302) 655-5000 Facsimile: (302) 658-6395
Counsel for Defendants Purepac Pharmaceutical Co. and Alpharma Inc.	

Barbara S. Wahl *(wahl.barbara@arentfox.com)* Richard J. Berman *(berman.richard@arentfox.com)* D. Jacques Smith *(smith.jacques@arentfox.com)* Janine A. Carlan *(carlanjanine@arentfox.com)* John K. Hsu *(hsu.john@arentfox.com)* **ARENT FOX PLLC** 1050 Connecticut Ave., N.W. Washington, D.C. 20036-5339 Telephone: (202) 857-6000 Facsimile: (202) 857-6395	Philip A. Rovner *(provner@potteranderson.com)* **POTTER ANDERSON & CORROON LLP** 1313 N. Market Street, Hercules Plaza, 6th Floor P.O. Box 951 Wilmington, DE 19899-0951 Telephone: (302) 984-6000 Facsimile: (302) 658-1192
Counsel for Defendants Par Pharmaceutical, Inc. and Par Pharmaceutical Companies, Inc.	

Stuart Sender (*ssender@budd-larner.com*) **BUDD LARNER** 150 John F. Kennedy Parkway Short Hills, NY 07078-0999 Telephone: (973) 315-4462 Facsimile: (973) 379-7734	Richard L. Horwitz (rhorwitz@potteranderson.com) **POTTER ANDERSON & CORROON LLP** Hercules Plaza P.O. Box 951 Wilmington, DE 19899 Telephone: (302) 984-6027 Facsímile: (302) 658-1192
Counsel for Defendants Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd.	

/s/ Mary B. Matterer

Mary B. Matterer # 2696
MORRIS JAMES HITCHENS & WILLIAMS LLP
222 Delaware Ave., 10th Floor
Wilmington, DE 19801
Telephone: (302) 888-6800
mmatterer@morrisjames.com

EXHIBIT A

Issued by the
UNITED STATES DISTRICT COURT

Southern DISTRICT OF New York

In re '318 Patent Infringement Litigation

V.

SUBPOENA IN A CIVIL CASE

CASE NUMBER: [1] 05-381 (KAJ) (Consolidated)

(Currently pending in the United States District Court for the District of Delaware)

TO: Custodian of Records
The Mount Sinai Hospital
One Gustave L Levy Place
New York. NY 10029

☐ YOU ARE COMMANDED to appear in the United States District Court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

☑ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case.

PLACE OF DEPOSITION	DATE AND TIME
Winston & Strawn LLP, 200 Park Avenue, New York, NY 10166-4193	April 28, 2006 at 9:30 a.m.

☑ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects):

(See attached Rider)

PLACE	DATE AND TIME
Winston & Strawn LLP, 35 West Wacker Drive, Chicago, IL 60601	April 15, 2006 at 9:00 a.m.

☐ YOU ARE COMMANDED to permit inspection of the following premises at the date and time specified below.

PREMISES	DATE AND TIME

Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. Federal Rules of Civil Procedure, 30(b)(6).

ISSUING OFFICER SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT)	DATE
Amy D. Brody, Attorney for Defendants Mylan Pharmaceuticals Inc. and Mylan Laboratories Inc.	March 29, 2006

ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER

Amy D. Brody, 6 West Hubbard Street, Suite 500, Chicago, Illinois, 60610. Telephone: (312) 222-6344

(See Rule 45, Federal Rules of Civil Procedure, Parts C & D on Reverse)

[1] If action is pending in district other than district of issuance, state district under case number.

PROOF OF SERVICE

DATE PLACE

SERVED

SERVED ON (PRINT NAME) MANNER OF SERVICE

SERVED BY (PRINT NAME) TITLE

DECLARATION OF SERVER

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on _____
DATE

_____
SIGNATURE OF SERVER

_____
ADDRESS OF SERVER

_____

Rule 45, Federal Rules of Civil Procedure, Parts C & D:

(c) PROTECTION OF PERSONS SUBJECT TO SUBPOENAS.

(1) A party or an attorney responsible for the issuance and service of a subpoena shall take reasonable steps to avoid imposing undue burden or expense on a person subject to that subpoena. The court on behalf of which the subpoena was issued shall enforce this duty and impose upon the party or attorney in breach of this duty an appropriate sanction which may include, but is not limited to, lost earnings and reasonable attorney's fee.

(2) (A) A person commanded to produce and permit inspection and copying of designated books, papers, documents or tangible things, or inspection of premises need not appear in person at the place of production or inspection unless commanded to appear for deposition, hearing or trial.

(B) Subject to paragraph (d)(2) of this rule, a person commanded to produce and permit inspection and copying may, within 14 days after service of subpoena or before the time specified for compliance if such time is less than 14 days after service, serve upon the party or attorney designated in the subpoena written objection to inspection or copying of any or all of the designated materials or of the premises. If objection is made, the party serving the subpoena shall not be entitled to inspect and copy materials or inspect the premises except pursuant to an order of the court by which the subpoena was issued. If objection has been made, the party serving the subpoena may, upon notice to the person commanded to produce, move at any time for an order to compel the production. Such an order to compel production shall protect any person who is not a party or an officer of a party from significant expense resulting from the inspection and copying commanded.

(3) (A) On timely motion, the court by which a subpoena was issued shall quash or modify the subpoena if it

(i) fails to allow reasonable time for compliance,

(ii) requires a person who is not a party or an officer of a party to travel to a place more than 100 miles from the place where that person resides, is employed or regularly transacts business in person, except that, subject to the provisions of clause (c)(3)(B)(iii) of this rule, such a person may in order to attend trial be commanded to travel from any such place within the state in which the trial is held, or

(iii) requires disclosure of privileged or other protected matter and no exception or waiver applies, or

(iv) subjects a person to undue burden.

(B) If a subpoena

(i) requires disclosure of a trade secret or other confidential research, development, or commercial information, or

(ii) requires disclosure of an unretained expert's opinion or information not describing specific events or occurrences in dispute and resulting from the expert's study made not at the request of any party, or

(iii) requires a person who is not a party or an officer of a party to incur substantial expense to travel more than 100 miles to attend trial, the court may, to protect a person subject to or affected by the subpoena, quash or modify the subpoena, or, if the party in whose behalf the subpoena is issued shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship and assures that the person to whom the subpoena is addressed will be reasonably compensated, the court may order appearance or production only upon specified conditions.

(d) DUTIES IN RESPONDING TO SUBPOENA.

(1) A person responding to a subpoena to produce documents shall produce them as they are kept in the usual course of business or shall organize and label them to correspond with the categories in the demand.

(2) When information subject to a subpoena is withheld on a claim that it is privileged or subject to protection as trial preparation materials, the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim.

RIDER

Definitions

1. "The Mount Sinai Medical Center" shall mean shall mean the Mount Sinai Hospital and Mount Sinai School of Medicine and any present or former employees, agents, representatives, subsidiaries or entities or persons acting on behalf of or that are deemed a part of The Mount Sinai Medical Center.

2. "Dr. Bonnie Davis" shall mean Dr. Bonnie Davis, the inventor of the '318 patent and former employee of Mount Sinai Hospital and the Bronx VA Hospital.

3. The '318 patent shall mean U.S. Patent No. 4,663,318, issued on May 5, 1987 and related Application No. 819,141. A copy of the '318 patent is attached hereto.

4. "Current Litigation" shall mean the lawsuit entitled *In re '318 Patent Infringement Litigation*, Civil Action No. 05-356-KAJ (consolidated), pending in the United States District Court for the District of Delaware.

5. "Related Litigation" shall mean any lawsuit filed by Janssen, Janssen, L.P. and/or Synaptech wherein Janssen, Janssen, L.P. and/or Synaptech assert the '318 patent.

6. "Galantamine" or “Galantamine Hydrobromide” shall mean the chemical compound (4a*S*,6*R*,8a*S*)-4a,5,9,10,11,12-hexahydro-3-methoxy-11-methyl-6*H*-benzofuro[3a,3,2-*ef*][2]benzazepin-6-ol hydrobromide, which is the active pharmaceutical ingredient in pharmaceutical products approved by the FDA for the treatment of mild to moderate dementia of the Alzheimer's type, also known as "Galanthamine."

7. "Invention Disclosure" shall mean any and all material submitted by or on behalf of Dr. Bonnie Davis to The Mount Sinai Medical Center relating to the use of galantamine hydrobromide to treat Alzheimer's disease and related dementia.

8. The terms "you" and "your" mean The Mount Sinai Medical Center, and any employees, agents, representatives, or persons acting on behalf of The Mount Sinai Medical Center.

9. The term communication means the transmittal of information (in the form of facts, ideas, inquiries or otherwise).

10. The term "document" or "documents" is used herein in a comprehensive sense as set forth in Rule 34(a) of the Federal Rules of Civil Procedure, and shall be defined to include, without limitation, all tangible things, all written, printed, typed, photocopies, photographic, graphic or recorded matter of any kind, any recorded material however produced or reproduced, including agreements, books, calendars, charts, contracts, communications, computer databases, computer memory media, computer printouts, correspondence, desk pads, diaries, drafts, drawings, entries in books of account, electronic mail, facsimile transmissions, files, folders, graphs, guidelines, instructions, lists, manuals, memoranda, minutes, notes, operating procedures, pamphlets, reports, rules studies, telegrams, teletypes, and all written or tangible things that can be derived from any computer database, microfilm, microfiche, or other storage medium. A draft or non-identical copy is a separate document within the meaning of this term.

11. The term "person" is defined as any natural person or any business, legal or governmental entity or association.

12. The term "concerning" means relating to, referring to, describing, evidencing, or constituting.

13. Something is "relating to" a subject if it makes a statement about, refers to, mentions, discusses, describes, reflects, deals with, consists of, constitutes, compromises,

concerns, evidences, records, or in any way pertains to the subject, either in whole or in part, and either directly or indirectly.

14. The terms "all" and "each" shall be construed as all and each.

15. The connectives "and" and "or" shall be construed either disjunctively or conjunctively as necessary to bring within the scope of discovery request all responses that might otherwise be construed to be outside it scope.

16. The use of the singular form of any word includes the plural and vice versa.

17. The term "including" means without limitation.

18. With respect to any document which you claim is privileged or otherwise immune from discovery, provide a list with the following information for each such document: (a) type (e.g., letter, memorandum, handwritten notes); (b) its date; (c) its author; (d) all addressees or recipients of the original or copies thereof; (e) its present location and custodian; (f) a brief description of its subject matter; (g) the nature of the privilege or immunity claimed; and (h) the paragraph of this request to which such document relates.

SCHEDULE A

REQUESTS FOR PRODUCTION OF DOCUMENTS

1. All documents from Dr. Bonnie Davis and/or anyone acting on her behalf, including but not limited to John Richards, to The Mount Sinai Medical Center relating to an Invention Disclosure.

2. All documents from The Mount Sinai Medical Center to Dr. Bonnie Davis and/or anyone acting on her behalf, including but not limited to John Richards, relating to an Invention Disclosure, including all documents relating to a March 6, 1987, letter from The Mount Sinai Medical Center to Dr. Bonnie Davis.

3. All documents relating to The Mount Sinai Medical Center's evaluation, analysis, and review of Dr. Bonnie Davis' alleged invention of using galantamine hydrobromide for the treatment of Alzheimer's Disease and related dementias.

4. All documents relating to the '318 patent.

5. All documents relating to the Current Litigation or any Related Litigation.

6. All documents relating to Dr. Kenneth Davis and the '318 patent.

7. All documents relating to Dr. Kenneth Davis and galantamine hydrobromide.

8. All documents relating to whether The Mount Sinai Medical Center has a claim to Dr. Bonnie Davis' alleged invention of using galantamine hydrobromide for the treatment of Alzheimer's Disease and related dementias as claimed in the '318 patent.

SCHEDULE B

DEPOSITION TOPICS

1. Identify and explain the materials reviewed by The Mount Sinai Medical Center to determine whether Dr. Bonnie Davis conceived of the invention claimed in the '318 patent prior to her appointment to the Mount Sinai faculty.

2. Explain the process used by The Mount Sinai Medical Center to determine whether Dr. Bonnie Davis conceived of the invention claimed in the '318 patent prior to her appointment to the Mount Sinai faculty.

3. Explain the involvement, duties and responsibilities of the individuals responsible for evaluating whether Dr. Bonnie Davis conceived of the invention claimed in the '318 patent prior to her appointment to the Mount Sinai faculty.

4. Explain the destruction or non-production of any documents otherwise responsive to Defendants' subpoena.

5. Identify and explain any communications between Dr. Bonnie Davis, Dr. Kenneth Davis and/or anyone acting on their behalf on the one hand, with the Mt. Sinai Medical Center on the other hand, relating to the '318 patent, any Invention Disclosure, and/or relating to the use of galantamine hydrobromide to treat Alzheimer's Disease and related dementias.

Exhibit A to Rider to Subpoena directed to The Mount Sinai Hospital

United States Patent [19]

Davis

[11] **Patent Number: 4,663,318**

[45] **Date of Patent: May 5, 1987**

[54] **METHOD OF TREATING ALZHEIMER'S DISEASE**

[76] Inventor: **Bonnie Davis**, 17 Seacrest Dr., Huntington, N.Y. 11743

[21] Appl. No.: **819,141**

[22] Filed: **Jan. 15, 1986**

[51] **Int. Cl.**[4] **A61K 31/55**

[52] **U.S. Cl.** **514/215**

[58] **Field of Search** 514/215

[56] **References Cited**

PUBLICATIONS

Chem. Abst. (81)-72615z (1974).
Chem. Abst. (86)-115157z (1977).
Horshenson et al. J. Med. Chem. vol. 29, No. 7, 7/86, pp. 1125-1130.
Kendall et al., J. Chem. & Hospital Pharmacol., (1985) 10-327-330.
S. Chaplygina et al., J. of Highest Nervous Activity vol. XXIV 1976 Issue 5, pp. 1-4.
Krause, J. of Highest Nervous Activity, vol. XXII, 1974, Issue 4.

Primary Examiner—Stanley J. Friedman
Attorney, Agent, or Firm—Ladas & Parry

[57] **ABSTRACT**

Alzheimer's disease may be treated with galanthamine.

7 Claims, No Drawings

JAN RAZ-0000001

METHOD OF TREATING ALZHEIMER'S DISEASE

GENERAL FIELD OF THE INVENTION

The present invention relates to a novel method of treating Alzheimer's disease and more particularly to a treatment using galanthamine.

BACKGROUND ART

Galanthamine and acid addition salts thereof have, for many years, been known to have anticholinesterase properties. Cozanitis in Anaesthesia 29 163-8 (1974) describes the effect of galanthamine hydrobromide on plasma cortisol of patients receiving relaxant anaesthesia and Cozanitis et al in Acta Anesth. Scand. 24:166-168 (1980) describe the effect of galanthamine on plasma ACTH values during anaethesia. These studies showed an increase in both plasma cortisol and plasma ACTH when galanthamine was administered to patients together with atropine.

Il'yuchenok et al (Chemical Abstracts 70 36296K describe the appearance of θ-rhythm on an electroencephalogram when galanthamine is administered intravenously to rabbits.

Increase in short-term memory in dogs by use of galanthamine is described by Krauz in Chemical Abstracts 81 72615Z.

The antagonistic effect of galanthamine to scopolamine-induced amnesia in rats is described by Chaplygina et al in Chemical Abstracts 86 115157Z, and in Zhurnal Vysshei Nervnoi Deiatelnosti imeni P. Pavlova (MOSKVA) 26:1091-1093, 1976.

Alzheimer's disease, presenile dementia, causes much distress not only to those suffering from the disease, but also those who are close to them. The custodial care of advanced victims of the disease is a tremendous expense to society. At present, there is no effective means of improving the functional status of persons with the disease.

It is an object of the present invention to improve the cognitive function of patients with Alzheimer's disease.

SUMMARY OF THE INVENTION

A method for treating Alzheimer's disease and related dementias which comprises administering to mammals, including humans, an effective Alzheimer's disease cognitively-enhancing amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof. A radioactively-labelled form of the molecule may also serve as a diagnostic test for Alzheimer's disease.

DETAILED DESCRIPTION OF THE INVENTION

Galanthamine can be administered in any convenient chemical or physcial form. For example, it may be administered as its hydrobromide, hydrochloride, methylsulfate or methiodide.

Galanthamine or its pharmaceutically-acceptable acid addition salts may be administered to a patient suffering from Alzheimer's disease orally or by subcutaneous or intravenous, injection, or intracerebroventricularly by means of an implanted reservoir. It may be necessary to begin at lower doses than are ultimately effective.

Galanthamine and its acid addition salts form crystals. They are in general only sparingly soluble in water

at room temperature and so injectible compositions are normally in the form of an aqueous suspension. If necessary, pharmaceutically-acceptable suspension aids may be employed. Typically, such a suspension will be employed at a concentration of 1-50 mg/ml more commonly 5-40 mg/ml, for example, 5-30 mg/ml or 10-40 mg/ml, typically 20-30 mg/ml of galanthamine. Typical dosage rates when administering galanthamine by injection are in the range 5-1,000 mg per day depending upon the patient. For example, divided doses in the range 0.5-5 mg/kg body weight per day may prove useful. Typically, one might administer a dosage of 50-300 mg per day to a patient of a body weight of 40-100 kg, although in appropriate cases such dosages may prove useful for patients having a body weight outside this range. In other cases, dosages as low as 10 mg and as high as 500 mg may be appropriate for persons in this body weight range.

Galanthamine or its pharmaceutically-acceptable acid addition salts may also be administered orally, for example, as an aqueous suspension or a solution in aqueous ethanol or as a solid such as a tablet or capsule. Suspensions or solutions for oral administration are typically of about the same concentration as those used for injections. However, it may be desirable when administering the drug orally to use a higher dosage rate than when administering it by injection. For example, dosages up to 2000 mg per day may be used, such as dosages in the range 100-600 mg per day. In preparing such tablets or capsules, standard tablet or capsulemaking techniques may be employed. The dosage rate of galanthamine or its pharmaceutically-acceptable salt will normally be in the same range as for oral administration of a liquid. If desired, a pharmaceutically-acceptable carrier such as starch or lactose may be used in preparing galanthamine tablets. Capsules may be prepared using soft galatine as the encapsulating agent. If desired, such capsules may be in the form of sustained release capsules wherein the main capsule contains microcapsules of galanthamine which release the contents over a period of several hours thereby maintaining a constant level of galanthamine in the patient's blood stream.

The following test provides a good animal model for Alzheimer's disease in humans: A selective lesion is placed in a subcortical nucleus (nucleus basalis of Meynert) with a resultant cortical cholinergic deficiency, similar in magnitude to that seen in early to moderate stage Alzheimer's disease. Numerous behavioral deficits, including the inability to learn and retain new information, characterizes this lesion. Drugs that can normalize these abnormalities would have a reasonable expectation of efficacyin Alzheimer's disease. Haroutunian, V, Kanof P, Davis, KL: Pharmacological alleviations of cholinergic-lesion-induced memory defects in rats. Life Sciences 37:945-952, 1985.

The following specific formulations may find use in treatment of Alzheimer's disease:

Tablets or capsules containing 5, 10 and 25 mg galanthamine hydrobromide to be taken four times a day, or a sustained-release preparation delivering an equivalent daily dose.

Parenteral solution containing 5 mg/ml.

Liquid formulation for oral administration available in 5 mg/5 ml and 25 mg/5 ml concentration.

There have been reports that galanthamine can cause cardiac arrythmias. In such cases, it may be desirable to

JAN RAZ-0000002

administer galanthamine in conjunction with another drug such as propanthelinbromide to control such arrythmias.

I claim:

1. A method of treating Alzheimer's disease and related dementias which comprises administering to a patient suffering from such a disease a therapeutically effective amount of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

2. A method according to claim 1, wherein the administration is parenteral at a daily dosage of 5–1,000 mg of galanthamine or a pharmaceutically-acceptable acid addition salt thereof.

3. A method according to claim 2, wherein said dosage rate is 50–300 mg per day.

4. A method according to claim 1, wherein said administration is oral and is in the range 10–2000 mg per day.

5. A method according to claim 4, wherein said dosage rate of 100–600 mg per day.

6. A method according to claim 1, wherein galanthamine is administered at a dosage rate of 0.1 to 4 mg/kg body weight of a patient, parenterally.

7. A method according to claim 1, wherein galanthamine is administered intracerebroventricularly via an implanted reservoir at a dosage rate of 0.01 to 5.0 mg/kg day.

* * * * *

JAN RAZ-0000003